

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.
Please amend claims 80 and 85.

Listing of Claims:

1. - 79. (Canceled)

80. (Currently Amended) A ligand-activated uni-molecular detector comprising:
a circularly permuted marker protein comprising a first interactor domain
covalently bonded to the circularly permuted marker protein through an N-terminal breakpoint
of the circularly permuted marker protein and a second interactor domain covalently bonded to
the circularly permuted marker protein through a C-terminal breakpoint **of the** circularly
permuted **[[of the]]** marker protein, wherein said circularly permuted marker protein is
functionally reconstituted only upon binding of said first interactor domain and said second
interactor domain to a single ligand.

81. (Previously Presented) The ligand-activated uni-molecular detector of claim
80, wherein said circularly permuted marker protein is a circularly permuted enzyme.

82. (Previously Presented) The ligand-activated uni-molecular detector of claim
81, wherein said circularly permuted enzyme is a β -lactamase protein.

83. (Previously Presented) The ligand-activated uni-molecular detector of claim
82, wherein said circularly permuted enzyme is a TEM-1 β -lactamase protein.

84. (Previously Presented) The ligand-activated uni-molecular detector of claim
80, wherein said N-terminal break point and said C-terminal break point are within a solvent
exposed loop between elements of secondary structure within the enzyme.

85. (Currently Amended) The ligand-activated uni-molecular detector of claim 80, wherein said circularly permuted protein [[is]] consists essentially of a β -lactamase protein with the following numbering convention:

His	Pro	Glu	Thr	Leu	Val	Lys	Val	Lys	Asp	Ala	Glu	Asp	Gln	Leu	Gly
26				30					35					40	
Ala	Arg	Val	Gly	Tyr	Ile	Glu	Leu	Asp	Leu	Asn	Ser	Gly	Lys	Ile	Leu
				45					50					55	
Glu	Ser	Phe	Arg	Pro	Glu	Glu	Arg	Phe	Pro	Met	Met	Ser	Thr	Phe	Lys
				60					65					70	
Val	Leu	Leu	Cys	Gly	Ala	Val	Leu	Ser	Arg	Ile	Asp	Ala	Gly	Gln	Glu
				75					80					85	
Gln	Leu	Gly	Arg	Arg	Ile	His	Tyr	Ser	Gln	Asn	Asp	Leu	Val	Glu	Tyr
				90					95					100	
Ser	Pro	Val	Thr	Glu	Lys	His	Leu	Thr	Asp	Gly	Met	Thr	Val	Arg	Glu
									110					115	
Leu	Cys	Ser	Ala	Ala	Ile	Thr	Met	Ser	Asp	Asn	Thr	Ala	Ala	Asn	Leu
									125					130	
Leu	Leu	Thr	Thr	Ile	Gly	Gly	Pro	Lys	Glu	Leu	Thr	Ala	Phe	Leu	His
									140					145	
Asn	Met	Gly	Asp	His	Val	Thr	Arg	Leu	Asp	Arg	Trp	Glu	Pro	Glu	Leu
									155					160	
Asn	Glu	Ala	Ile	Pro	Asn	Asp	Glu	Arg	Asp	Thr	Thr	Met	Pro	Val	Ala
									170					175	
Met	Ala	Thr	Thr	Leu	Arg	Lys	Leu	Leu	Thr	Gly	Glu	Leu	Leu	Thr	Leu
									190					195	
Ala	Ser	Arg	Gln	Gln	Leu	Ile	Asp	Trp	Met	Glu	Ala	Asp	Lys	Val	Ala
									205					210	
Gly	Pro	Leu	Leu	Arg	Ser	Ala	Leu	Pro	Ala	Gly	Trp	Phe	Ile	Ala	Asp
									220					225	

Lys Ser Gly Ala Gly Glu Arg Gly Ser Arg Gly Ile Ile Ala Ala Leu
235 240 245
Gly Pro Asp Gly Lys Pro Ser Arg Ile Val Val Ile Tyr Thr Thr Gly
250 255 260 265
Ser Gln Ala Thr Met Asp Glu Arg Asn Arg Gln Ile Ala Glu Ile Gly
270 275 280
Ala Ser Leu Ile Lys His Trp
285

(SEQ ID NO: 2);

~~comprising amino acids 1 to 263 of SEQ ID: NO 2~~, wherein said N-terminal breakpoint and said C-terminal breakpoint are within 10 amino acids of an amide bond junction between two amino acids selected from the group consisting of asparagine 52 and serine 53, leucine 91 and glycine 92, glutamine 99 and asparagine 100, proline 174 and asparagine 175, glutamic acid 197 and leucine 198, lysine 215 and valine 216, alanine 227 and glycine 228, and glycine 253 and lysine 254.

86. (Previously Presented) The ligand-activated uni-molecular detector of claim 85, wherein said two amino acids are selected from the group consisting of proline 174 and asparagine 175, glutamic acid 197 and leucine 198, lysine 215 and valine 216, alanine 227 and glycine 228, and glycine 253 and lysine 254.

87. (Previously Presented) The ligand-activated uni-molecular detector of claim 85, wherein said two amino acids are glutamic acid 197 and leucine 198.

88. (Previously Presented) The ligand-activated uni-molecular detector of claim 80, wherein said ligand is a protein ligand.

89. (Previously Presented) A method of detecting the presence of a target ligand using a ligand-activated uni-molecular detector comprising the steps of:

(a) contacting said target ligand with said ligand-activated uni-molecular detector, said ligand-activated uni-molecular detector comprising a circularly permuted marker protein comprising a first interactor domain covalently bonded to the circularly permuted marker protein through an N-terminal breakpoint of the circularly permuted marker protein and a second interactor domain covalently bonded to the circularly permuted marker protein through a C-terminal breakpoint of the circularly permuted marker protein;

(b) allowing said target ligand to bind to said first interactor domain and said second interactor domain;

(c) after step (b), allowing said circularly permuted marker protein to functionally reconstitute;

(d) detecting the functionally reconstituted circularly permuted marker protein thereby detecting the presence of said target ligand.